Clinical Update

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The Dynamics of Oral Lichen Planus and Lichenoid Mucositis

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Introduction

Lichenoid mucositis is a noncommittal term referring to a wide range of mucosal lesions which closely mimic oral lichen planus both clinically and histologically, yet may represent a different pathoetiology altogether. In general, most oral lichenoid reactions represent a common end point in response to a myriad of extrinsic agents (drugs, allergens) or altered immunologically-mediated mucocutaneous processes.

The clinical appearance of lichenoid mucositis is often described as having a gray to white interlacing reticular pattern set within an erythematous background (Figure 1). Focal atrophic erythematous areas exhibiting central ulceration with a peripheral radiating pattern of hyperkeratotic striae may be observed. In addition, keratotic plaques can be present which may create a diagnostic dilemma in clinically differentiating from a bona-fide leukoplakia[1]. Clinically, it is not unusual for a patient to present with multiple patterns[2].

Oral lichen planus, a relatively common and perhaps underrecognized mucocutaneous disorder, shares many clinical and histologic features within the spectrum of the "lichenoid mucositis" diagnostic umbrella. Due to the variable morphologies of oral lichen planus, one must consider a broad differential diagnosis and have a thorough understanding of the multifaceted clinical presentations. Definitive diagnosis often requires a strong clinical correlation, thorough medical history review and supportive histopathology.

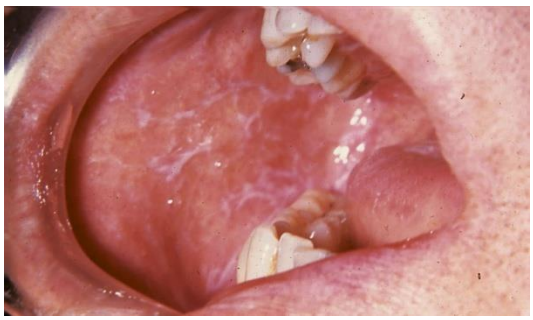

Figure 1. The reticular pattern of lichen planus is more common and is typically asymptomatic.

Oral Lichen Planus

Oral lichen planus (OLP) is a relatively common immune-mediated disease of unknown etiology[3] affecting 0.1% to 4% of the population with a predilection for females[4]. OLP often occurs bilaterally on the buccal mucosa, followed by the palate, gingiva and vermilion border of the lip. Clinical presentation can vary from gray to white lacy, reticular striae (so-called striae of Wickham) to painful erythema and ulcerations. The more common reticular lesions are typically asymptomatic and may wax and wane over time. Patients with erosive lichen planus often complain of moderate to severe discomfort which can interfere with eating and hygiene[2]. Occasionally erosive lichen planus may be confined to the gingival mucosa, producing a clinical appearance of desquamative gingivitis.

Although the etiology of oral lichen planus is still considered idiopathic, a review of the data suggests that Langerhan cells or keratinocytes present antigen to CD4+ (helper) T cells which are then stimulated to secrete cytokines IL2 and interferon gamma, which activate CD8+ (cytotoxic) T cells that ultimately cause apoptosis of basilar keratinocytes in the affected epithelium[5].

The salient histopathologic features of OLP are relatively distinct and consist of a band-like infiltrate of lymphocytes subjacent to the basilar epithelium (Figure 2). The epithelium forms a "saw tooth" pattern (Figure 3) and may vary from hyperplastic and hyperkeratotic to atrophic, which corresponds to the variable erythematous and keratotic clinical appearance.

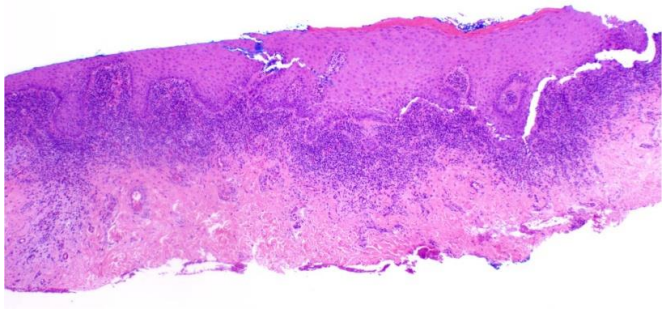

Figure 2. Low power magnification of oral lichen planus shows a band-like infiltrate at the epithelial-connective tissue interface.

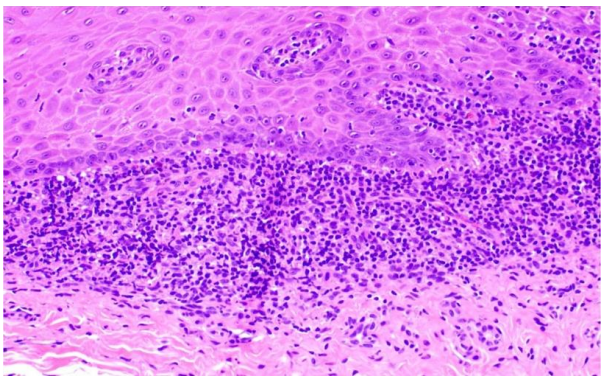

Figure 3. High power magnification reveals "saw tooth" pattern of epithelial rete ridges classically associated with lichen planus.

Treatment of OLP is palliative in nature; painful lesions that may interfere with nutrition or hygiene can typically be managed with topical steroids. Clobetasol propionate 0.05% applied twice daily for up to two months is considered the treatment of choice[1]. Tacrolimus 0.1% ointment is currently being explored as a treatment method and shows promising results[6].

Lichenoid Drug Reaction

Many systemic medications can cause oral lichenoid drug reactions which may be indistinguishable from OLP both clinically and histologically[2,3]. Unlike OLP, lichenoid drug eruptions typically present as a single lesion[7]. Oral hypoglycemics, angiotensin-converting enzyme (ACE) inhibitors and non-steroidal anti-inflammatory drugs

(NSAIDs) are some of the more common drugs implicated[1]. A table of select drugs is provided (Table 1).

Table 1. Select Medications implicated in Lichenoid Drug Reactions[8]

• Allopurinol	• Methyldopa
• Amphotericin	• Penicillamine
• Captopril	• Propranolol
• Carbamazepine	• Pyritinol
• Dapsone	• Quinidine
• Hydroxychloroquine	• Spironolactone
• Ketoconazole	• Streptomycin
• Lithium	• Sulfonureas
• Lorazepam	• Tetracycline

Lichenoid drug reactions can be difficult to differentiate and treat due to their morphologic similarities to OLP. Some authors have suggested minor histologic differences to aid in identifying drug-related lesions: a mixed inflammatory infiltrate is present with perivascular inflammation as opposed to the predominantly lymphocytic population seen in OLP and a more diffuse infiltrate versus band-like[3,7]. This is not a consistent finding and is not considered diagnostic for lichenoid drug reactions[1]. These lesions can occur even years after the patient initiates the drug[9] which may create more difficulty in identifying a suspected drug. The only reliable means by which to treat this condition is also how the diagnosis is validated – taking the patient off the suspected drug to observe resolution of lesion(s), a method that may be impractical for patients taking multiple medications. Additionally, a patient's drug regimen may have required years of modifications by a physician who may be reluctant to change medications, especially considering many of the alterative medications may cause the same lichenoid lesions[3].

Oral Lichenoid Contact Reaction

Oral lesions related to dental restorative materials are not uncommon and are often associated with metallic dental appliances and restorative materials which present as a localized allergic reaction of the oral mucosa[10] (Figure 4).

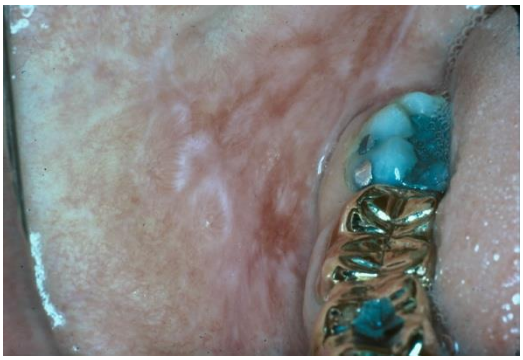

Figure 4. An atrophic, erythematous lesion with a surrounding white, radiating hyperkeratotic striae on the buccal mucosa juxtaposed to molars with gold and amalgam restorations.

Cinnamic aldehyde, a flavoring compound found in cinnamon-flavored gums, toothpastes and mouth rinses, is also known to cause lichenoid mucositis. Due to the proximity of the lesion to the offending material, a causal relationship can often be identified clinically and when the offending agent is removed, the lesions quickly resolve[7].

Other Considerations

There are a host of additional mimics of lichenoid mucositis which require clinical correlation to elucidate the etiology. In addition to the topics covered, the differential diagnosis includes but is not necessarily limited to the following:

- Squamous cell carcinoma or epithelial dysplasia, especially when lesions are located on higher risk sites such as the lips, floor of mouth or lateral tongue. Mixed erythematous and keratotic lesions in these sites should be biopsied unless an obvious cause is identified. In cases where a lesion does not resolve within 10 days of removing the suspected agent, biopsy is required.
- Candidiasis can present in the oral cavity and resemble lichenoid mucositis, especially the erythematous, chronic multifocal and hyperplastic forms[8] of which the white plaques do not wipe off. The diagnosis can be established by biopsy or exfoliative cytology.
- Lupus erythematosus is the most common connective tissue disease in the United States and primarily affects women over 30 years old[8]. Oral lesions develop in approximately 40% of these patients and in most cases appear identical to erosive forms of lichen planus[8]. Skin lesions (including a butterfly malar rash) and a recent history of weight loss, fatigue and fever can accompany these oral lesions. The biopsy will reveal more specific characteristic features that, when combined with a complete medical history, can allow for the diagnosis of lupus erythematosus.
- Graft-versus-host-disease is a major complication of allogeneic bone marrow transplantation and affects 25-70% of recipients[11]. Although the pathogenesis is not completely understood, GVHD is believed to be caused by donor T lymphocytes reacting to tissue antigens in recipient cells[1]. Oral manifestations may include painful ulcerative lesions, lichenoid mucositis, xerostomia and salivary gland atrophy[11].

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